

We claim:

1. A method for changing binding strength of an isolated force-activated bond stress-dependent adhesion molecule (I-FABSDAM) to a force-activated bond stress-dependent binding ligand (FABSDB-L) for said I-FABSDAM, said method comprising changing a bond stress on said I-FABSDAM wherein said binding strength increases when said bond stress increases and decreases when said bond stress decreases.
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2. The method of claim 1 wherein said bond stress is caused by a shear force.
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3. The method of claim 1 wherein said bond stress is a tensile force.
4. The method of claim 1 comprising increasing said bond stress whereby said binding strength is increased.
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5. The method of claim 1 comprising decreasing said bond stress whereby said binding strength is decreased.
6. The method of claim 2 wherein said method results in said I-FABSDAM being tightly bound to said FABSDB-L.
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7. The method of claim 1 wherein said I-FABSDAM is selected from the group consisting of adhesins, selectins, integrins, cadherins, immunoglobulin superfamily cell adhesion molecules, and syndecans that are capable of binding in a force-activated bond stress-dependent manner.
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8. The method of claim 7 wherein said adhesin comprises a FimH polypeptide, or the lectin domain of a FimH polypeptide.
- 30 9. The method of claim 8 wherein said FimH polypeptide is an *E. coli* FimH polypeptide.
10. The method of claim 6 wherein said I-FABSDAM comprises a polypeptide having the sequence of Genbank Accession Number P08191.

11. The method of claim 6 wherein said FimH polypeptide is engineered.
12. The method of claim 6 wherein said FimH polypeptide is a FimH-f18 polypeptide derived from the *E. coli* strain f18.

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13. The method of claim 12 wherein said FimH-f18 polypeptide is engineered to comprise a valine at amino acid position 27.
14. The method of claim 6 wherein said FimH polypeptide comprises an amino acid substitution selected from the group consisting of a proline at position 154, a proline at position 155, a proline at position 156, a leucine at position 32, and an alanine at position 124.

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15. The method of claim 8 wherein said FimH polypeptide is FimH-j96.

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16. The method of claim 1 wherein said FABSDB-L comprises mannose or fructose.
17. The method of claim 16 wherein said mannose is selected from the group consisting of monomannose, trimannose, and oligomannose.

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18. The method of claim 1 wherein said I-FABSDAM is attached to a particle selected from the group consisting of bacterial pili, naturally occurring isolated molecules, synthetic molecules, proteins, polypeptides, organelles, prokaryotic cells to which said I-FABSDAM is not native, eukaryotic cells to which said I-FABSDAM is not native, viruses, organisms, nanoparticles, and microbeads, microparticles, or a surface selected from the group consisting of cell membranes, device surfaces and a synthetic substrate surfaces.

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19. The method of claim 18 wherein said FABSDB-L is also attached to said particle.

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20. The method of claim 1 wherein said FABSDB-L is attached to a particle selected from the group consisting of bacterial pili, isolated molecules, synthetic molecules, proteins, polypeptides, organelles, prokaryotic cells to which said I-FABSDAM is not native, eukaryotic cells to which said I-FABSDAM is not native, viruses, organisms,

nanoparticles, microparticles and microbeads or a surface selected from the group consisting of cell membranes, device surfaces and synthetic substrate surfaces.

21. The method of claim 20 wherein said I-FABSDAM is also attached to said particle.

5 22. The method of claim 1 wherein changing said bond stress comprises applying a bond stress between a bond stress dependence lower threshold of said I-FABSDAM and a bond stress dependence upper threshold of said I-FABSDAM.

10 23. The method of claim 1 wherein changing said bond stress comprises applying a bond stress between about 0.01 dynes/cm² and about 100 dynes/cm².

24. The method of claim 1 wherein changing said bond stress comprises applying a bond stress between about .05 dynes/cm² and about 20 dynes/cm².

15 25. The method of claim 1 wherein changing said bond stress comprises applying a bond stress between about 0.1 dynes/cm² and about 10 dynes/cm².

20 26. The method of claim 1 applied to a system wherein a first component of said system comprises a plurality of said I-FABSDAMs attached to a first object, wherein a second component of said system comprises a plurality of said FABSDB-Ls attached to a second object, and wherein said I-FABSDAMs and FABSDB-Ls are capable of binding to each other in a force-activated bond stress-dependent manner, and wherein said method comprises increasing bond stress on said I-FABSDAMs, resulting in said first component changing from being unbound to said second component to being bound to said second component.

25 27. The method of claim 1 applied to a system wherein a first component of said system comprises a plurality of said I-FABSDAMs attached to a first object, wherein a second component of said system comprises a plurality of said FABSDB-Ls attached to a second object, and wherein said I-FABSDAMs and FABSDB-Ls are capable of binding to each other in a force-activated bond stress-dependent manner, and wherein said method comprises decreasing bond stress on said I-FABSDAMS, resulting in said first component changing from being bound to said second component to being unbound from said second component

28. The method of claim 1 applied to a system wherein a first component of said system comprises a plurality of said I-FABSDAMs attached to first particles, and a second component of said system comprises a plurality of said FABSDB-Ls attached to second particles, said method comprising homogenously mixing said first and second components, then increasing said bond stress on said system, whereby a substantially uniform material comprising complexes of said first components with said second components is formed.

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10 29. The method of claim 28 further comprising cross-linking said substantially uniform material once said complexes have been formed by increasing said bond stress.

15 30. The method of claim 1 wherein a plurality of said I-FABSDAMs are attached to a first selected surface of a plurality of first selected three-dimensional forms, wherein a plurality of FABSDB-Ls are attached to second selected surface of a plurality of second selected three dimensional forms, and wherein said changing is increasing, thereby resulting in said first and second forms self-assembling into a selected geometric pattern.

20 31. The method of claim 30 wherein said first form is the same as said second form.

32. The method of claim 31 wherein said first and second forms are cylinders, wherein said first and second surfaces are the curved sides of said cylinders, and said geometric pattern is a layer composed of said cylinders.

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33. The method of claim 32 wherein said layer is a synthetic membrane.

34. The method of claim 30 wherein said first and second forms are cylinders, wherein said first and second surfaces are the flat ends of said cylinders, and said geometric pattern is a chain composed of said cylinders.

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35. The method of claim 34 wherein said first form has said I-FABSDAMs attached thereto but does not have FABSDB-Ls capable of binding said I-FABSDAMs attached thereto; wherein said second form has said FABSDB-Ls attached thereto but does not have

FABSDAMs capable of binding said FABSDB-Ls attached thereto; and said geometric pattern is an alternating link chain.

36. The method of claim 30 wherein said first and second forms are cylinders, wherein
5 each cylinder comprises a first flat end and a second flat end, wherein said first flat ends are attached to said I-FABSDAMs and said second flat ends are attached to said FABSDB-Ls, and said geometric pattern is a directional chain composed of said cylinders.

10 37. The method of claim 1 performed in a fluid-containing channel, wherein a plurality of said I-FABSDAMs and said FABSDB-Ls are attached to particles or surfaces and are present in an amount sufficient to clog said channel when said I-FABSDAMs and said FABSDB-Ls are bound to each other, said method comprising changing said bond stress on said I-FABSDAMs whereby said binding strength of said I-FABSDAMs and
15 FABSDB-Ls is changed, whereby the flow rate of said fluid through said channel or the pressure drop is changed.

20 38. The method of claim 37 wherein said bond stress is increased causing said I-FABSDAMs and FABSDB-Ls to be bound to each other, whereby said flow rate is decreased.

25 39. The method of claim 37 wherein said bond stress is decreased causing said I-FABSDAMs and FABSDB-Ls to be unbound to each other, whereby said flow rate is increased.

40. The method of claim 37 wherein said I-FABSDAMs and/or said FABSDB-Ls are bound to particles.

30 41. The method of claim 37 wherein said I-FABSDAMs or said FABSDB-Ls are bound to a wall of said channel.

42. The method of claim 37 wherein said channel is in fluid communication with a fluid exit port and a bypass port, wherein changing said bond stress changes the amount of fluid flowing through said exit and bypass ports.

43. A method for removing a target particle from a fluid comprising:

- (a) adding to said fluid a target particle binding agent, said target particle binding agent being attached to a first member of a FABSDAM/FABSDB-L pair;
- (b) adding to said fluid the second member of a FABSDAM/FABSDB-L pair attached to a removing agent;
- (c) allowing said target particle binding agent to bind said target particle;
- (d) applying a bond stress to said FABSDAM to allow force-activated bond stress-dependent binding of said first pair member and said second pair member, thereby forming a complex comprising said target particle, said target particle binding agent attached to said first pair member, and said second pair member attached to said removing agent; and
- (e) removing said complex from said fluid.

44. The method of claim 43 wherein step (e) comprises a step selected from the group consisting of sedimentation, filtration, bioseparation, applying an electric force, and applying a magnetic force.

45. The method of claim 43 wherein said target particle is selected from the group consisting of pollutant particles, toxin particles, and drug particles.

46. The method of claim 43 wherein said target particle binding agent is an antibody.

47. A method for separating first FABSDB-Ls from second FABSDB-Ls, wherein said FABSDB-Ls are in a fluid, wherein said FABSDB-Ls are capable of binding to FABSDAMs in a force-activated bond stress-dependent manner, and wherein said first and second FABSDB-Ls induce different bond stresses on said FABSDAM under the same conditions, said method comprising:

- (a) contacting said fluid with an amount of said FABSDAMs sufficient to bind substantially all of said first FABSDB-Ls, wherein said FABSDAMs are attached to a removing agent;
- (b) applying a bond stress to said FABSDAMs sufficient to cause binding of said first FABSDB-Ls to said FABSDAMs to form a complex, said bond stress

being insufficient to cause binding of said second FABSDB-Ls to said FABSDAMs; and

- (c) removing said complex comprising said first FABSDB-Ls, and FABSDAMs and said removing agent from said fluid.

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48. The method of claim 47 wherein said removing agent consists of particles capable of responding to a removing force.

49. The method of claim 45 also comprising:

- 10 (a) contacting said fluid with said FABSDAMs attached to a removing agent in an amount sufficient to bind to substantially all of said second FABSDB-Ls;
- (b) applying a second bond stress to said FABSDAMs sufficient to cause binding of said second FABSDB-Ls to said FABSDAMs to form a second complex; and
- (c) separating said second complex comprising said second FABSDB-L from said 15 fluid.

50. The method of claim 49 wherein said second bond stress is selected so as to cause selective binding of said FABSDAMs to said second FABSDB-Ls, to the exclusion of other components in said fluid.

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51. The method of claim 47 wherein said first FABSDB-Ls differ from said second FABSDB-Ls in a characteristic selected from the group consisting of magnetic and electric charge, mass, and three-dimensional form.

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52. The method of claim 47 also comprising a step of covalently linking said FABSDB-Ls to said removing agent.

53. A fluidic device comprising a surface having a plurality of I-FABSDAMs attached thereto.

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54. The device of claim 53 wherein said surface is a channel wall surface or portion thereof.

55. The device of claim 53 wherein said surface is that of a component selected from the group consisting of a channel, a parallel plate flow chamber, a cylindrical channel, a microfluidic channel, and a cell sorter.

5 56. A method for selectively releasing into a fluid first FABSDA-Ls from a plurality of FABSDAMs to which first and second FABSDA-Ls are stress-dependently bound, and wherein when said FABSDA-Ls are bound to said FABSDAMs under bond stress, said first and second FABSDA-Ls induce different bond stresses on said FABSDAMs under the same fluid flow conditions, said method comprising:

10 (a) contacting said fluid with said FABSDAMs bound to said SDDB-Ls; and
(b) changing the bond stress on said FABSDAMs by an amount sufficient to cause release of said first FABSDA-Ls into said fluid, but insufficient to cause release of said second FABSDA-Ls into said fluid.

15 57. A method for selectively concentrating first FABSDA-Ls from second FABSDA-Ls, wherein said FABSDA-Ls are in a fluid, wherein said FABSDA-Ls are capable of binding to FABSDAMs in a force-activated bond stress-dependent manner, and wherein said first and second FABSDA-Ls induce different bond stresses on said FABSDAM under the same conditions, said method comprising:

20 (a) contacting said fluid with an amount of said FABSDAMs sufficient to bind substantially all of said first FABSDA-Ls, wherein said FABSDAMs are attached to a removing agent;
(b) applying a bond stress to said FABSDAMs sufficient to cause binding of said first FABSDA-Ls to said FABSDAMs to form a complex, said bond stress being insufficient to cause binding of said second FABSDA-Ls to said FABSDAMs; and
(c) removing said complex comprising said first FABSDA-Ls and FABSDAMs and said removing agent from said fluid.

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30 58. A method for measuring the rate of flow of a fluid comprising:
(a) adding a plurality of FABSDAMs or FABSDA-Ls to said fluid;
(b) placing a plurality of FABSDAMs capable of binding to said FABSDA-Ls or a plurality of FABSDA-Ls capable of binding to said FABSDAMs in contact with said fluid;

(c) allowing said FABSDAMs and said FABSDB-Ls to bind in a force-activated bond stress-dependent manner; and

(d) detecting and quantitatively measuring the amount of binding of said FABSDAMs to said FABSDB-Ls;

5 wherein said amount of binding is indicative of the rate of flow of said fluid.

59. The method of claim 58 wherein said plurality of FABSDAMs or FABSDB-Ls placed in contact with said fluid are bound to a substrate.

10 60. The method of claim 59 wherein said substrate is a channel wall in contact with said fluid.

61. The method of claim 60 wherein said channel is a microchannel.

15 62. The method of claim 58 wherein said step of detecting and quantitatively measuring comprises measuring light scattering of said fluid.

63. A method for delivering a particle to a surface of a system, said surface having attached thereto one member of an I-FABSDAM/FABSDB-L pair, said system also comprising a fluid in contact with said surface, said method comprising:

20 (a) adding to said fluid the other member of said pair attached to said particle; and

(b) allowing said pair members to bind in a force-activated bond stress-dependent manner.

25 64. A bond stress-activated valve for controlling a fluid flow rate in a channel, said channel having a surface in contact with said fluid, said channel surface having attached thereto a plurality of a first member of an I-FABSDAM/FABSDB-L pair, said fluid comprising a plurality of the second member of said pair, wherein said first and second members are present in an amount sufficient to clog or partially clog said channel when bound in complexes in a force-activated bond stress-dependent manner.

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65. The valve of claim of 64 which is a microvalve, wherein said channel is a microchannel.

66. The valve of claim of 64 wherein said fluid has a first flow rate through said channel, wherein when said first flow rate changes a bond stress on said I-FABSDAMs, said change resulting in a binding strength change in the binding of said I-FABSDAMs and said FABSDB-Ls, thereby changing said flow rate.

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67. A bond stress-activated adhesive system comprising:

- (a) a plurality of I-FABSDAMs; and
- (b) a plurality of FABSDB-Ls capable of binding to said I-FABSDAMs in a bond stress dependent manner.

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68. The bond stress-activated adhesive system of claim 67 wherein said I-FABSDAMs are attached to a surface of a film.

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69. The bond stress-activated adhesive system of claim 68 wherein said FABSDB-Ls are also attached to said film, whereby said film is capable of adhering in a force-activated bond stress-dependent manner to itself.

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70. The bond stress-activated adhesive system of claim 68 wherein said FABSDB-Ls are attached to a second film whereby said second film is capable of adhering in a force-activated bond stress-dependent manner to said first film.

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71. A method for making a bond stress-activated adhesive system comprising:

- (a) attaching a first member of an I-FABSDAM/FABSDB-L pair to a surface of a first film; and
- (b) attaching the second member of said pair to a surface of a second film.

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72. A viscosity modifier comprising a plurality of I-FABSDAMs and a plurality of FABSDB-Ls, said I-FABSDAMs and FABSDB-Ls being capable of binding to each other in force-activated bond stress-dependent manner.

73. A method for modifying the viscosity of a fluid comprising:

- (a) adding to said fluid a plurality of I-FABSDAMs;
- (b) adding to said fluid a plurality of FABSDB-Ls capable of binding in a shear stress-dependent manner to said I-FABSDAMs; and

(c) changing a bond stress on said I-FABSDAMs.

74. A method for interfering with the force-activated bond stress-dependent binding of a FABSDAM and a FABSDB-L capable of binding to said FABSDAM in a force-activated bond stress-dependent manner, said method comprising contacting said FABSDAM with an antibody capable of binding said FABSDAM but incapable of binding to a FABSDB-L-binding domain of said FABSDAM; and allowing said antibody to bind said FABSDAM.

10 75. The method of claim 74 wherein said FABSDAM is a FimH polypeptide, wherein said antibody is capable of binding to a domain of said FimH polypeptide selected from the group consisting of FimH amino acids 25-31 (SEQ ID NO: 1), FimH amino acids 110-123 (SEQ ID NO: 2), and FimH amino acids 150-160 (SEQ ID NO: 3).

15 76. A monoclonal antibody generated using, and capable of binding to, a polypeptide having an amino acid sequence selected from the group consisting of FimH amino acids 25-31 (SEQ ID NO: 1), FimH amino acids 110-123 (SEQ ID NO: 2), and FimH amino acids 150-160 (SEQ ID NO: 3).

20 77. A polyclonal antibody generated using, and capable of binding to, a polypeptide having an amino acid sequence selected from the group consisting of FimH amino acids 25-31 (SEQ ID NO: 1), FimH amino acids 110-123 (SEQ ID NO: 2), and FimH amino acids 150-160 (SEQ ID NO: 3).

25 78. An antibody generated using, and capable of binding to, the force-activated structure of a FABSDAM polypeptide.

79. An immunogenic composition comprising a polypeptide having an amino acid sequence selected from the group consisting of FimH amino acids 25-31 (SEQ ID NO: 1), FimH amino acids 110-123 (SEQ ID NO: 2), and FimH amino acids 150-160 (SEQ ID NO: 3).

30 80. The immunogenic composition of claim 79 wherein said polypeptide is produced synthetically.

81. A method for making an engineered FimH polypeptide having different force-activated bond stress-dependent binding strength to a selected FABSDB-L than a natural FimH polypeptide, said method comprising engineering a DNA sequence encoding a FimH polypeptide to encode an engineered FimH polypeptide and expressing said engineered FimH polypeptide, wherein said engineered polypeptide comprises an amino acid substitution at an amino acid position selected from positions 154-156, position 32, and position 124.

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82. The method of claim 81 comprising engineering a codon selected from the group consisting of codons encoding valine at positions 154, 155, and 156 to encode proline.

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83. The method of claim 81 comprising engineering the codon encoding glutamine at position 32 to encode a leucine and engineering the codon encoding serine at position 124 to encode an alanine.

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84. A FimH polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, and SEQ ID NO:12.

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85. A method for changing binding strength of an isolated force-activated bond stress-dependent adhesion molecule (I-FABSDAM) to a force-activated bond stress-dependent binding ligand (FABSDB-L) for said I-FABSDAM, said method comprising changing a bond stress on said I-FABSDAM; wherein said binding strength increases when said bond stress decreases and decreases when said bond stress increases; wherein said bond stress is between an upper force-activated bond stress-dependent threshold of said I-FABSDAM and a higher force-activated bond stress-dependent binding threshold of said I-FABSDAM.

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